

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently Amended) An array reader $[(110)]$ suitable for clinical purposes for reading a two-dimensional array $[(103)]$ of features on a planar substrate $[(302)]$, in which the features carry photo-responsive markers, the markers capable of emitting light upon excitation, the array reader comprising:

an illumination system $[(120)]$ for simultaneously exciting multiple photo-responsive markers distributed in a two-dimensional array over the substrate,

and an image collection and recording system $[(140)]$ having a field of view for emissions from the features on the substrate,

wherein the illumination system $[(120)]$ comprises a light source in the form of at least one light-emitting diode arranged to flood the two-dimensional array $[(103)]$ with light at an excitation wavelength, along an illumination path $[(P)]$ disposed at an angle (θ) between about 20° and 50° to the plane of the substrate,

the image collection and recording system $[(140)]$ having an image-acquiring axis $[(141)]$ substantially normal to the plane of the substrate $[(102)]$ carrying the array, employing a two-dimensional sensor $[(146)]$ comprising a solid-state array (203, Fig. 4) of photosensitive elements, elements, e.g. a charge coupled device (CCD) or a CMOS array, and the image collection and recording system constructed ~~constructed~~ and arranged to apply an image of the array of features upon the solid-state array of size $[(D_c)]$ of the same order of magnitude as the size $[(D_o)]$ of the array, e.g. within a range of magnification of up to about 25% or reduction down to 75%, the image collection and recording system $[(140)]$ having an

intermediate numerical aperture NA to enable recording the image of fluorescence from the excited two-dimensional array with clinical accuracy and without translation of the array.

2. (Cancelled)

3. (Currently Amended) The array reader of claim 1 [[or 2]] in which the image collection and recording system has an effective aperture between $NA=0.3$ and $NA=0.60$; ~~preferably the value of NA being between about 4.0 and 5.5.~~

4-5. (Cancelled)

6. (Currently Amended) The illumination system of claim 1 [[5]] constructed and arranged to provide excitation illumination over the two-dimensional array [[(103)]] on the substrate [[(102)]] of a power density greater than 30 mW/cm^2 .

7. (Cancelled)

8. (Currently Amended) The array reader of ~~any of the foregoing~~ claim[[s]] 1 in which the field of view [[(V)]] of the array reader has a diameter [[(D_o)]] of the order of 10 mm or more.

9. (Cancelled)

10. (Currently Amended) The array reader of ~~any of the foregoing~~ claim[[s]] 1 constructed and arranged to deliver to said solid state sensor array [[(203)]] an image of the field of view that is not magnified.

11. (Currently Amended) The array reader of ~~any of the foregoing claim~~[[s]] 1 constructed and arranged to deliver to said solid state sensor array an image of the field of view reduced between about 30% and 50%.

12-13. (Cancelled)

14. (Currently Amended) The array reader of ~~any of the foregoing claim~~[[s]] 1 in combination with a carrier [[[102]]] for the array comprising a substrate layer [[[302]]] carried by a support body [[[306]]], said image collection and recording system [[[140]]] residing on the same side of the substrate as does the array of features such that the path [[(P)]] of said illumination reaches said array [[[103]]] before reaching the support body[[(306)]], said carrier constructed to absorb excitation radiation penetrating beyond said layer.

15. (Currently Amended) The array reader of claim 14 in which said support body [[[306]]] is transparent, ~~e.g. glass,~~ and between said substrate layer [[[302]]] and said transparent body [[[306]]] resides a substantially opaque adherent layer [[[304]]] capable of substantially blocking excitation radiation tending to enter the transparent body.

16. (Currently Amended) The array reader of claim 15 in which said substantially opaque layer [[[304]]] comprises a layer of metal oxide.

17. (Currently Amended) The array reader of claim 1 in which said substrate [[[302]]] is in the form of a transparent layer carried by a transparent body[[(306)]], the image collection and recording system [[[140]]] lying beyond the transparent body on the same side of the array as the transparent body.

18. (Currently Amended) The array reader of ~~any of the foregoing claim~~[[s]] 1 in combination with a carrier [[[102]]] for said array [[[103]]] that comprises ~~an ultra-thin~~ substrate

layer $[(302)]$ on a support body, $[i.e.]$ the substrate having a thickness less than about 5 micron, ~~preferably less than about 3 micron.~~

19. (Currently Amended) The array reader of ~~any of the foregoing~~ claim $[s]$ 1 in which said array $[(103)]$ is disposed on a substrate $[(302)]$ comprising a clear layer of nitrocellulose ~~or polystyrene.~~

20. (Cancelled)

21. (Currently Amended) The array reader of ~~any of the foregoing~~ claim $[s]$ 1 in combination with a substrate $[(302)]$ carrying excitation energy reference features $[(166)]$ distributed across said two-dimensional array of features, said image collection and recording system $[(140)]$ including a normalizing arrangement (~~see Fig. 10~~) for normalizing data detected in the vicinity of respective reference features based on the quantity of detected emission from the respective reference features.

22. (Currently Amended) The array reader of ~~any of the foregoing~~ claim $[s]$ 1 in which said illumination system $[(120)]$ comprises at least two different light source sub-systems (402, 412, 406; 404, 414, 408, ~~see Fig. 7A~~) respectively of substantially different wavelengths, each associated with a respective optical system delivering light along a path, the paths of said sub-systems to said substrate lying along respectively different axes, the axes being spaced apart about said substrate.

23. (Cancelled)

24. (Currently Amended) The array reader of ~~any of the foregoing~~ claim $[s]$ 1 in which said illuminating system includes light source $[s]$ diodes (~~e.g. diodes 402, 404~~) selected respectively to excite Cy3 and Cy5, and said image collection and recording system $[(140)]$

includes changeable band-pass filters (424, 424', Fig. 7A) suitable to permit passage of emissions respectively from Cy3 and Cy5 or a single band-pass filter ~~[(424)]~~ is provided suitable to permit multiple band-pass ~~emission such as both band-pass~~ emissions of Cy3 and Cy5.

25. (Cancelled)

26. (Currently Amended) The array reader of ~~any of the foregoing claims~~ claim 1 in which said illumination system includes a diode light source ~~[(132)]~~ followed by ~~[[and]]~~ a homogenizer (130, Fig. 2B) effective to reduce variation in flux density across the field of illumination.

27-38. (Cancelled)

39. (Currently Amended) A fluorescence reader-based diagnostic method for a disease for which there is a set of known protein biomarkers in blood or other body constituent, comprising the steps of (1) providing a two-dimensional array ~~[(103)]~~ of different reagents on a substrate, the reagents respectively specific to bind members of a set of said biomarkers capable of diagnosing the disease, (2) exposing the array to fluorophore-labeled blood or body-constituent extract of an individual containing the biomarkers if present in the individual's blood or body constituent, (3) while the array is stationary, exciting the array by simultaneously illuminating the entire two-dimensional array by light ~~(e.g. by 120, Fig. 1)~~ at fluorophore-excitation wavelength employing dark field illumination, (4) capturing a fluorescence image of the entire two-dimensional excited array on a single frame of an imager comprising a solid state array, ~~e.g. by 140, Fig. 1)~~ and (5) analyzing the fluorescence image for the presence of the disease ~~(e.g. by computer 104, Fig. 1)~~.

40. (Cancelled)

41. (Currently Amended) The method of claim 39 ~~or 40~~ in which fluorescence intensity reference features $[(164)]$ are distributed through the array and the detected radiation from said bio-markers is normalized by the reader based on the response of said references to said illumination.

42-44. (Cancelled)

45. (Currently Amended) A method of reading an array on a substrate having features that include fluorophores, in which the array includes intensity calibration features of fluorescing character generally proportional in emission intensity to their illumination over the range of operable illumination intensities, including, forming an image of the array employing an array reader, and normalizing recorded array data during the reading of the array from nearby intensity calibration features within the array.

46-50. (Cancelled)